REMARKS:

Response to Rejections under 35 U.S.C. § 112

Claims 2-9, 13-27, 30 and 33 have been rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. The Examiner acknowledges that the specification is enabling for a method of treating hyperproliferative cells *in vitro* comprising the administration of an inhibitor of a receptor tyrosine kinase ligand, but asserts that the specification does not provide enablement for a method of treating hyperproliferative cells *in vivo* comprising the administration of an inhibitor of a receptor tyrosine kinase ligand. Applicants respectfully disagree.

The term "inhibitor" used according to the invention is characterized by a functional feature, namely, by the fact that the inhibitor inhibits a receptor tyrosine kinase ligand. Moreover, in the examples, the present specification provides appropriate tests for determining whether a compound is able to inhibit a receptor tyrosine kinase ligand as claimed. Therefore, testing of potential candidate compounds does not constitute an unacceptable burden for the person skilled in the art, in particular, because a large number of compounds can be excluded even before testing based on the knowledge and skill of that person.

The Examiner refers to a number of references in support of a presumption of unpredictability with regard to cancer therapeutics. Applicants do not agree that the set of references chosen as evidence of unpredictability are proper against the present invention. For example, the Examiner refers to Ezzell (J. NIH Res 1995) as "a review of the current thinking" in cancer that states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective and that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the growth of

micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p. 48, paragraph 6). It can be argued that the opinions and "bets" of immunologists in 1995 are not a proper reference in the rapidly advancing field of immunology. Moreover, on page 49, the concluding sentence of Ezzell is a quote from an immunologist, Dr. Srivastava, stating that current developments in cancer immunology could not have been imagined five years prior [to the article] and what comes next is anybody's guess". Thus, it is clear from Ezzell that the field of cancer vaccines has been rapidly progressing. The present specification provides disclosure on page 9, line 11 to page 11, line 24 that would enable one of skill in the art to determine proper dosages and to administer inhibitors of receptor tyrosine kinase ligands. Thus, based on the above, Applicants submit that the present specification does not lack enablement and request that the rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

Response to Rejections under 35 U.S.C. § 102

Claims 2, 15-18, 22, 26-27, and 30-33 have been rejected under 35 U.S.C. §102(b) as being anticipated by Tang et al. (U.S. 5,773,459). The Examiner asserts that Tang discloses the administration of the compound of formula ##STR3## for the treatment of hyperproliferative disorders. Applicants respectfully disagree.

Tang is directed to administering urea and thiourea compounds to inhibit tyrosine kinase activity. Thus, the hyperproliferative disorder treated by Tang is not therapy-resistant and the inhibitor of Tang is directed to inhibiting tyrosine kinase. There is no disclosure in Tang of a method of preventing or treating a therapy-resistant hyperproliferative disorder comprising administering an inhibitor of a receptor tyrosine kinase ligand. Thus, Applicants submit that the

subject matter of the present claims is novel and inventive in view of Tang and request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Claims 2, 15-18, 22, 26-27, and 30-33 have been rejected under 35 U.S.C. §102(e) as being anticipated by Uckun et al. (U.S. 6,864,286). The Examiner asserts that Uckun discloses administering a compound that inhibits the EGF receptor tyrosine kinase. While this may be correct, Applicants submit that the disclosure of Uckun is not relevant to the patentability of the present claims.

Uckun discloses a method of inhibiting EGFR tyrosine kinase comprising administering a leflunomide analog. There is no disclosure in Uckun of a method of preventing or treating a therapy-resistant hyperproliferative disorder comprising administering an inhibitor of a receptor tyrosine kinase ligand. Thus, Applicants submit that the subject matter of the present claims is novel and inventive in view of Uckun and request that the rejection under 35 U.S.C. §102(e) be withdrawn.

Claims 2-5, 15-18, 22, 26-27, and 30-33 have been rejected under 35 U.S.C. §102(e) as being anticipated by Agus (U.S. 7,384,940). The Examiner asserts that Agus discloses a method of increasing the sensitivity of treatment that has become resistant to receptor tyrosine kinase inhibitors comprising administering a kinase inhibitor that surmounts the receptor tyrosine kinase resistance. While this may be correct, Applicants submit that the disclosure of Agus is not relevant to the patentability of the present claims.

Agus is directed to administering a kinase inhibitor selected from the group consisting of gefitinib or a pharmaceutically acceptable salt thereof. There is no disclosure in Agus of a

method of preventing or treating a therapy-resistant hyperproliferative disorder comprising administering an inhibitor of a receptor tyrosine kinase ligand. Thus, Applicants submit that the subject matter of the present claims is novel and inventive in view of Agus and request that the rejection under 35 U.S.C. §102(e) be withdrawn.

Claims 2, 6, 8-9, 15-19, 22, 26-27, and 30-33 have been rejected under 35 U.S.C. §102(e) as being anticipated by Lee (U.S. 6,537,988). The Examiner asserts that Lee discloses a method of treating cancer comprising the use of combination therapy by administering a combination of receptor tyrosine kinase inhibitor and a chemotherapeutic. While this may be correct, Applicants submit that the disclosure of Lee is not relevant to the patentability of the present claims.

Lee is directed to administering a benzodiazepine derivative to inhibit tyrosine kinase activity. There is no disclosure in Lee of a method of preventing or treating a therapy-resistant hyperproliferative disorder comprising administering an inhibitor of a receptor tyrosine kinase ligand. Thus, Applicants submit that the subject matter of the present claims is novel and inventive in view of Lee and request that the rejection under 35 U.S.C. §102(e) be withdrawn.

Claims 2, 15-17, 23-25, and 30-33 have been rejected under 35 U.S.C. §102(e) as being anticipated by Majumdar (U.S. 6,582,934). The Examiner asserts that Majumdar discloses a method of using nucleic acid molecules for the treatment of cancer comprising administering a nucleic acid that inhibits EGFR, which attenuates EGFR kinase activity. While this may be correct, Applicants submit that the disclosure of Majumdar is not relevant to the patentability of the present claims.

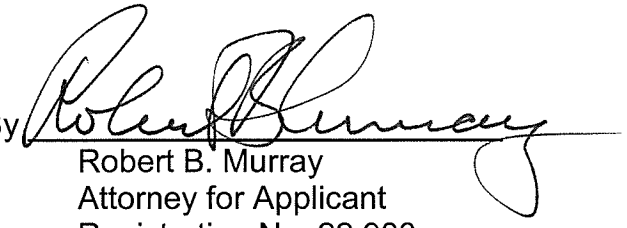
There is no disclosure in Majumdar of a method of preventing or treating a therapy-resistant hyperproliferative disorder comprising administering an inhibitor of a receptor tyrosine kinase ligand. Thus, Applicants submit that the subject matter of the present claims is novel and inventive in view of Majumdar and request that the rejection under 35 U.S.C. §102(e) be withdrawn.

Conclusions

In view of the above remarks, Applicants believe that all of the Examiner's rejections set forth in the September 5, 2008 Office Action have been fully overcome and that the present claims fully satisfy the patent statutes. Applicants, therefore, believe that the application is in condition for allowance. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

By 

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